BEACON trial

Best systemic treatments for adults with **a**topi**c** eczema over the l**on**g term

Co-Chief Investigators: Prof Catherine Smith and Dr Andrew Pink

Co-applicants: Prof Hywel Williams, Prof Max Parmar, Prof Richard Emsley, Prof Nick Reynolds, Prof Tracey Sach, Dr Jo Chalmers, Dr Stephen Smith, Dr Paul Leighton, Caroline Murphy, Angela Cape, Andy Proctor, Amanda Dougan, Tim Burton, Jack Kelly

Funded by the National Institute for Health Research (NIHR HTA)

Conflicts of interest

- I have received educational support from/ been a speaker/ advisor/ investigator for:
  - Lilly, Pfizer, Abbvie, Sanofi, Leo, Galderma, Novartis, Almirall, La Roche Posay, Janssen, UCB, BMS, Amgen, Celgene.

Aims and objectives

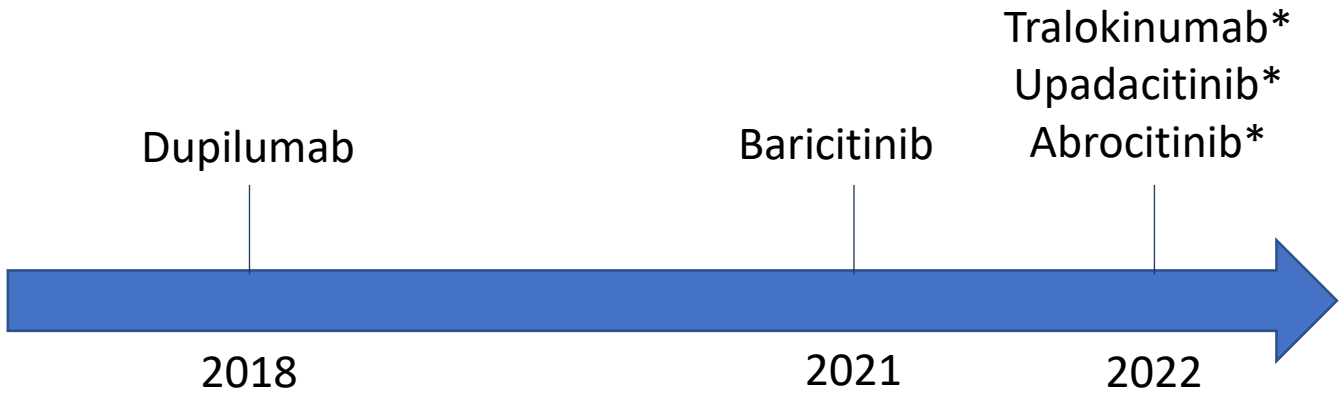
- Aim:
  - Provide an overview of the BEACON trial

- Objectives:
  - Overview of the systemic therapeutic landscape in adult eczema
  - Rationale for BEACON
  - BEACON trial design
  - Planned synergies/ add ons
  - Timelines

Current systemic treatment for adult eczema

Traditional systemic therapies

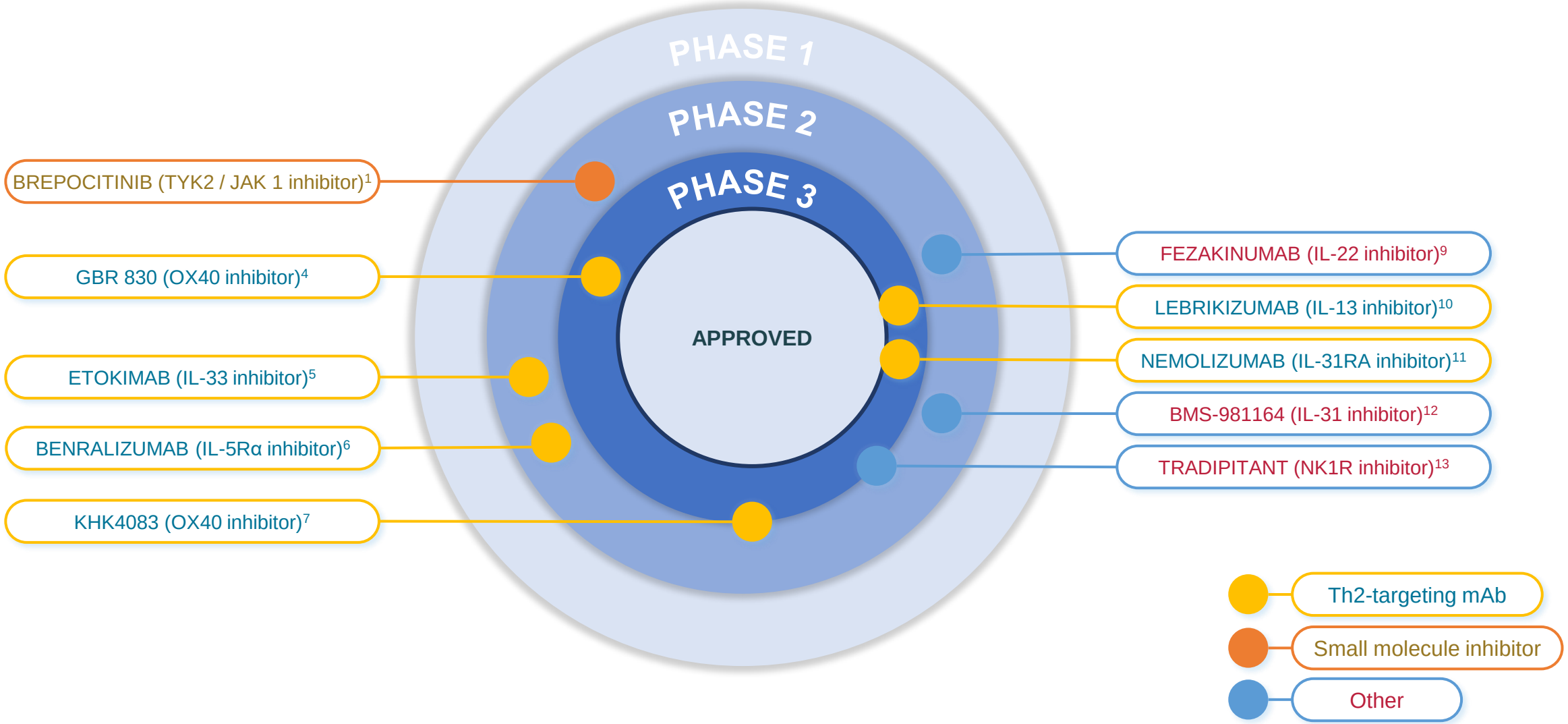
Ciclosporin
Methotrexate[+]
Azathioprine [+]
Mycophenolate mofetil [+]



[+] Not licensed

* Licensed but not NICE approved

Many more systemic treatments are coming…



BEACON trial

Background

- We do not know how the current systemic therapies for adult eczema compare in terms of their effectiveness, tolerability and cost-effectiveness

Aim

- **To determine the effectiveness, tolerability and cost-effectiveness of methotrexate, dupilumab and a Janus kinase inhibitor (JAKi, TBC) compared to ciclosporin in adults with moderate-severe atopic eczema**.

Primary hypotheses

- i) Dupilumab is superior to ciclosporin, ii) methotrexate is superior to ciclosporin and iii) JAKi is superior to ciclosporin.
    - *Only in the event that two of methotrexate, dupilumab or JAKi prove superior will they be compared with each other.*

UK, multicentre, 1 year, assessor-blind, randomised controlled trial

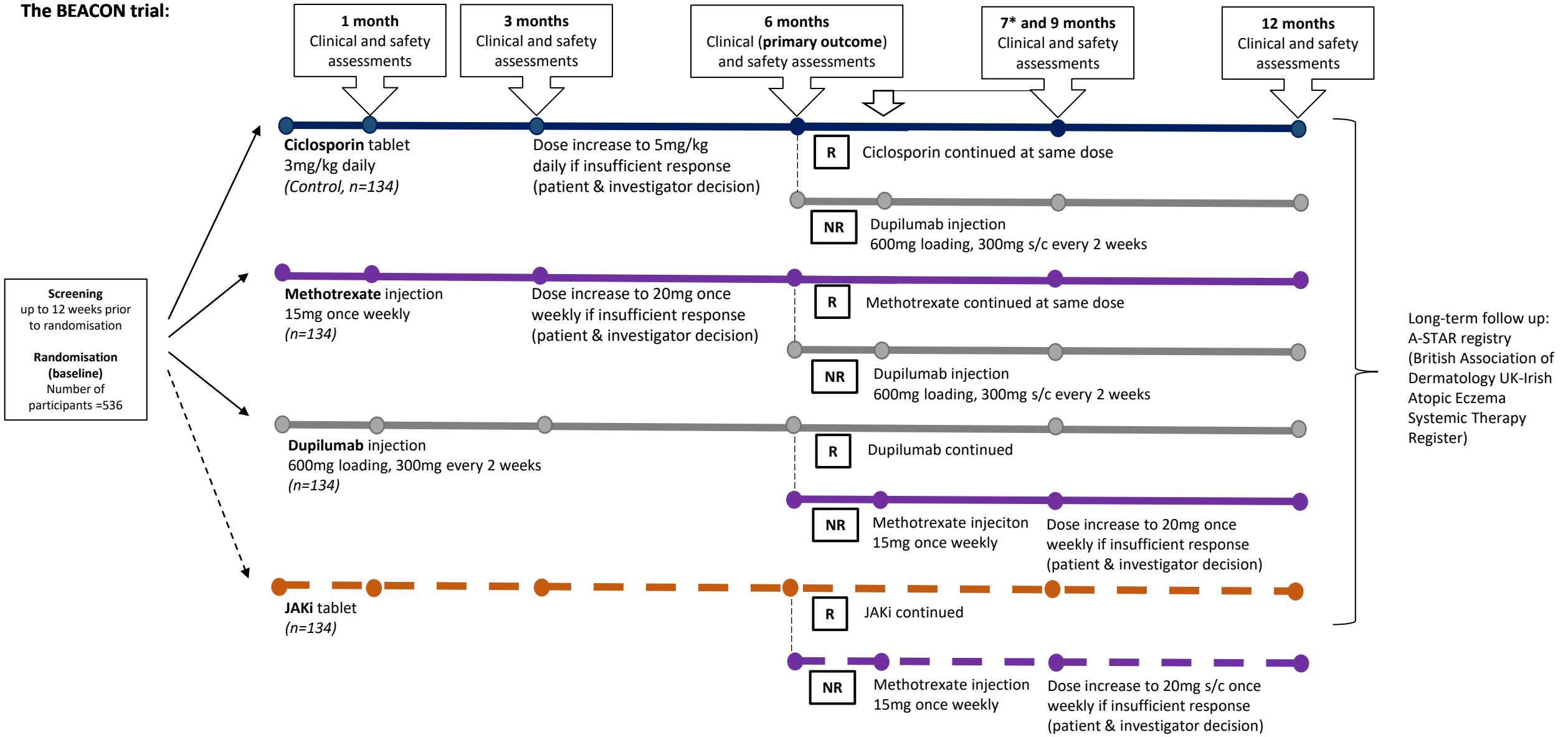
BEACON trial design

- **Study population:**
  - ***Adults with moderate-severe eczema requiring systemic therapy***
- Key inclusion criteria:
  - Adults (18 +); Eczema; Investigator Global Assessment (IGA) score of ≥3 (“moderate-severe”); requiring systemic therapy
- Key exclusion criteria:
  - Prior exposure to dupilumab, methotrexate, JAKi or ciclosporin; phototherapy or systemic immunomodulators 4 weeks prior to baseline; pregnant or breast feeding; patients in whom dupilumab, JAKi, methotrexate or ciclosporin are contraindicated.

- **Planned interventions:**

- **Ciclosporin (control),** tablet, 3mg/kg orally daily (increasing to 5mg/kg after 3 months if required)
- **Methotrexate,** injection, 15mg once weekly (increasing to 20mg after 3 months if required)
- **Dupilumab,** injection, 600mg week 0 followed by 300mg every two weeks
- **JAKi TBC**, oral

The BEACON trial:



R = responder (achieved EASI50 **and** DLQI reduction ≥4 and patient/ investigator happy to continue)

NR = non-responder (not achieved EASI50 **and** DLQI reduction ≥4)

Footnotes:

- Topical treatment permitted throughout, dose reduction (MTX, CiA, JAKi) permitted as per standard clinical care
- Additional safety bloods and blood pressure conducted 2/6/8 weeks after starting ciclosporin and 2/4 weeks post-increment
- Additional safety bloods conducted 2 weeks after starting or switching to methotrexate and 2/4 weeks post-increment
- * Only required for those who switch therapy, virtual review

Outcome measures

- **Primary outcome (6 months):**
  - **Objective eczema severity** - blinded assessor, measured using the Eczema Area Severity Index (EASI)

- **Secondary outcomes (measured at 1, 3, 6, 9, 12 months):**
  - Objective eczema severity
  - Patient reported symptoms (including itching, sleep disturbance, bleeding, weeping, oozing, cracking, flaking, dryness)
  - Disease control
  - Patient global assessment
  - Quality of life
  - Depression and anxiety
  - Cost-effectiveness
  - How safe/ tolerable the treatments are

Incorporating all Harmonising Outcome Measures for Eczema (HOME) recommended outcome domains

Remote digital capture of patient reported outcomes (PROMS)

Sample size and timetable

Sample size

- Designed to test separate comparisons of methotrexate, dupilumab and JAKi (TBC) for superiority against ciclosporin
- To detect a mean absolute difference of 6.6 (minimal clinically important difference) in EASI the **total sample size is 536 (134 per group)***.

Project timetable

- **48 months in total (planned start date Q3 2022)**: 24 months recruitment, 12 months follow up, 6 months analysis and close out.
- **Requiring 54 sites** to recruit 536 participants over 24 months

* Assuming SD of 13.6, 20% loss to follow up, 90% power, conservative type 1 error rate of 2.5% per comparison.
  - This will have 94% power to test a difference between methotrexate/dupilumab/abrocitinib of 6.6, 90% for a difference of 6 points, and 80% for 5.2 points.

Current sites:

Guy's & St Thomas	BSUH NHS Trust, Brighton Sussex
Newcastle	Ipswich hospital, East Suffolk and North East Essex NHS Foundation Trust
Southampton	
Manchester	Chapel Allerton, Leeds
Oxford	Epsom and St Helier
Edinburgh	Exeter
Cardiff	Aberdeen Royal infirmary, moving to Raigmore
Derby/ Burton	Singleton Hospital Swansea
Ninewells, Dundee	Beckenham Beacon (King's College Hospital south sites)
Russell's Hall Hospital, Dudley and potentially UHB	Homerton Hospital
Norfolk and Norwich	SWFT South Warwickshire Trust
Glasgow	Chester
Liverpool	Luton
Addenbrookes	County Durham and Darlington NHS Trust
York	Imeperial College Healthcare NHS Trust
Portsmouth	Torbay Hospital
Nottingham	Bath
Royal London	St Georges
King's College Hospital	Plymouth
Kirkcaldy (Fife)	East Suffolk & North Essex
Belfast	Lewisham & Greenwich NHS Trust
Walsall Manor	

N = 43, we need more! If you can help, contact me

Trial designs are constantly evolving…

STAMPEDE

Multi-arm multi-stage platform trial (prostate cancer)

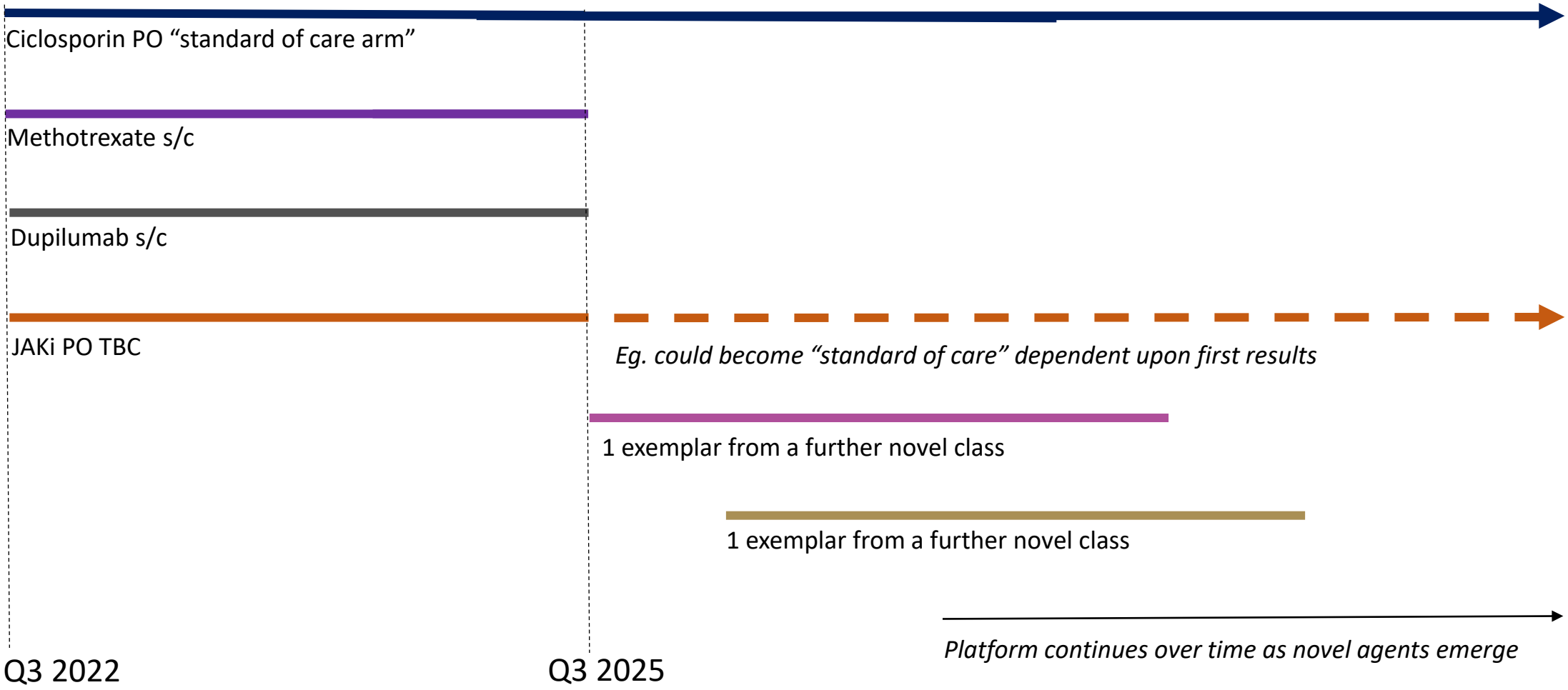
Max Parmar

RECOVERY

Randomised Evaluation of COVID-19 Therapy

BEACON has been set up as a platform, enabling the addition of more treatments in the future

Multi-arm multi-stage platform trial: adaptive trial design



Synergies

- Want to work in harmony with A-STAR
  - Dual consent
  - Continuation in A-STAR for long term follow up

- BEACON-OMICS study
  - What are the critical events that mediate drug outcomes?
    - *Identify shared mechanisms of action*
  - What are the determinants of variable treatment outcomes?
    - *Identify molecular determinants of treatment outcomes*

Summary

- **This trial will provide the first comprehensive head to head evidence on the comparative effectiveness, tolerability and cost effectiveness of the three (fourth TBC) key systemic agents used to treat moderate-severe adult eczema**

Summary

- **This trial will provide the first comprehensive head to head evidence on the comparative effectiveness, tolerability and cost effectiveness of the three (fourth TBC) key systemic agents used to treat moderate-severe adult eczema**
- Will inform the optimal treatment pathway over 12 months
- Will translate into improved health outcomes, minimise treatment switching, and enable healthcare commissioning based on clinical evidence and value for money.
- It has been designed such that new emerging treatments can be added in the future (platform)
- Work closely with A-STAR
- Provide samples for an exciting parallel mechanistic study

The BEACON team

Study leads:
Programme lead: Prof Catherine Smith
Chief Investigator: Dr Andrew Pink
Lead methodologist: Prof Richard Emsley

Co-applicants:
Prof Hywel Williams
Prof Max Parmar
Prof Nick Reynolds
Prof Tracey Sach,
Dr Jo Chalmers
Dr Stephen Smith
Dr Paul Leighton
Caroline Murphy
Angela Cape

Trial manager:
Jatinder Bisla

PPI co-applicants:
Tim Burton
Jack Kelly
Amanda Dougan
Andrew Proctor (National Eczema Society)

Funder: NIHR | National Institute for Health Research

Sponsors: Guy's and St Thomas' NHS Foundation Trust; King's College London

Partners: UK Dermatology Clinical Trials Network; MRC Clinical Trials Unit; St. John's Institute of Dermatology

www.beacontrial.org

andrew.pink@gstt.nhs.uk